A Petition for extension of time and a check for the requisite fee accompany response. Any fees which may be due in connection with this or any attached paper may be charged to Deposit Account No. 10-0447 (Reference. No.: 50657-05302USP1).

Claims 1-14, 17 and 18 are pending in the application. Claims 1-14, 17 and 18 are rejected. Claims 1 and 5 have been amended. Appendix A at page 13 of this Response lists all claims after amendment for Examiner's convenience.

The amendment to claim 1 and claim 5 incorporates the claim limitations from pending claims 2, 3 and 4. Support for this amendment can be found at page 18, lines 6-25, page 19, lines 1-25, and page 20, lines 1-2.

The second amendment to claim 5 deletes "RANTES" from the claim language.

RESPONSE TO OBJECTIONS TO SPECIFICATION

The Specification is objected to because of certain informalities. In making the objection, the Examiner states the following:

> The disclosure is objected to because of the following informalities: The first paragraph contains errors. The serial number of the provisional application to which priority is claimed is not correct, nor is the continuity data. The correct serial number is 60/113672 and it was converted from an application that was a continuation in part of 08/808720.
> Appropriate correction is required.

Applicants respond as follows:

The specification has been amended according to Examiner's request to reflect the correct priority and continuity data for the present application.

RESPONSE TO REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 1-14, 17, and 18 are rejected under 35 U.S.C. § 112, first paragraph, as containing

subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In making the rejection, the Examiner states the following:

> Claims 1-5, 10-14, 17, and 18 are drawn to a genus, i.e polynucleotides encoding amino-terminal modified chemokines. Applicant has disclosed the functional characteristics of one species, met-SDF-1 beta, which exhibits an enhanced function relative to the native molecule, but has not disclosed sufficient species for the broad genus of any amino-terminal modified chemokine. The disclosure of this one member is insufficient to describe this genus. The disclosed species demonstrates enhanced function as compared to the previously described, naturally produced chemokine, but applicant has not described the features of amino-terminally modified chemokines crucial to the this enhancement of function, such as specific structural or functional characteristics, and allowed modifications, that would identify the modified SDF-1 beta as being representative of a genus of amino-terminally modified chemokines. Claims 1-14, 17, and 18 encompass sequences comprising polynucleotides encoding amino-terminal modified chemokines and claims 6-9 additionally encompass sequences encoding fragments of modified chemokines. However, since the required structural and functional characteristics of the claimed genus have not been described, there is no way to determine what additional sequences would be tolerated for a given polynucleotide comprising one of the claimed sequences to be identifiable as a member of this genus. There is thus insufficient guidance regarding structural features that could identify other species in the claimed genus and one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Applicants respond as follows:

Applicants respectfully disagree with Examiner's conclusion that the specification discloses only one amino-terminal modified chemokine. The objective standard for determining compliance with the written description requirement is "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gostelli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with **reasonable** clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. (Emphasis added).

Applicants have provided four separate examples of amino-terminal modified chemokines under Example 1, page 42, including, met-hSDF-1α, met-hSDF-1β, GroHEK/hSDF-1α, and GroHEK/hSDF-1β. The method for producing amino-terminal modified chemokines is described under Example 1, in a detailed enough manner to facilitate the production of any amino-terminal modified chemokine. *See* page 42, lines 13-25, and page 43, line 1. The disclosure of four separate examples of amino-terminal modified chemokines satisfies the requirement that the applicant "convey with **reasonable** clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention."

Claims 1-14, 17, and 18 are also rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for polynucleotides encoding met-SDF-1 beta does not reasonably provide enablement for any other amino-terminally modified chemokines. In making the rejection, the Examiner states the following:

> The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims.
> As written, claims 1, 2, 5, 10-14, 17, and 18 encompass any change to the amino terminus of the listed chemokines, including additions, deletions, and substitutions. Claims 3 and 4 are drawn to specific modifications. Claims 6-9 are drawn to sequences comprising specific sequences, as well as sequences comprising fragments of these sequences, and complements. Claims 17 and 18 include further functional limitations. However applicant has not described the structural features or functional characteristics that would enable one of skill to make and use polynucleotides encoding amino-terminally modified polypeptides other than met-SDF-1-beta, including sequences comprising this or any other sequence. The amino acid sequence of an encoded polypeptide determines its structural and functional properties, and predictability of what effect additions will have is complex and well outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited.

Applicants respond as follows:

Applicants respectfully disagree with Examiner's conclusions that the specification does not enable a person skilled in the art to practice the invention commensurate in scope with the claims. As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to entire scope of the claim, then the enablement requirement of 35 U.S.C. § 112 is satisfied. *In re Fisher*, 427 F.2d 833, 839 (C.C.P.A. 1970). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt,* 537 F.2d 498, 504 (C.C.P.A. 1976).

Applicants have provided working examples for the expression and purification of four different amino-terminal modified chemokine proteins, and have further shown the use of met-hSDF-1β in the stimulation of calcium flux by amino-terminal-modified chemokines (Example 2), stimulation or inhibition of chemotaxis by amino-terminal-modified chemokines (Example 3), binding of chemokine to receptor after incubation with amino-terminal-modified chemokines (Example 4), down-modulation of chemokine receptor by amino-terminal-modified chemokine binding (Example 5), and the use of amino-terminal modified chemokines to inhibit HIV infection of cells (Example 6). These working examples provide detailed explanation for the use of any amino-terminal modified chemokine in the same context as met-hSDF-1β in Examples 2-6. The working examples are intended to illustrate preferred embodiments of the invention, and are not intended to limit the scope of the invention. The representative examples are detailed enough to inform one of ordinary skill in the art that the claimed genus can be used in the context of a specific example without undue experimentation.

Examiner has stated that "the applicant has not described the structural features or functional characteristics that would enable one of skill to make and use polynucleotides encoding amino-terminally modified polypeptides other than met-SDF-1-beta." In order to use the present invention in a manner that is commensurate with the scope of the claims, one of ordinary skill in the art does not need to know the structural features or functional characteristics of an amino-terminal modified chemokine. Under § 2164.02 of the Manual of Patent Examining Procedure, proof of enablement for other members of a claimed genus is required only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation. By merely stating that "the applicant has not described the structural features or functional characteristics that would enable one of skill to make and use polynucleotides encoding amino-terminally modified polypeptides other than met-SDF-1-beta," Examiner has not met her burden under § 2164.02 of establishing "that a person skilled in the art could not use the genus as a whole without undue experimentation." The invention as claimed does not require knowledge of the structural and functional characteristics of the amino-terminal modified chemokines in order to practice the claimed invention.

RESPONSE TO REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-14, 17 and 18 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In making the rejection, the Examiner states the following:

> The use of the laboratory names in claims 1-5, dependent claims 10-14, and claims 17 and 18 is vague and indefinite because the proteins are only described by arbitrary names or the designation "chemokine". While the names themselves may have some notion of the activity of

the proteins, there is nothing in the claims that distinctly identifies the proteins... Applicant should particularly point out definitive characteristics associated with the proteins and refer to them by the numbers of entered sequences.
Claims 1, 2, 6-14, 17, and 18 are indefinite in the recitation of "amino-terminal-modified". This term could encompass additions and deletions of any length, as well as substitutions, and thus the metes and bounds of this phrase are not clearly set forth in the claims.
Claim 6-9 are indefinite in the recitation of "amino-terminal fragment" and of "hybridizing under stringent conditions". Applicant has not described the length or specific characteristics of a "fragment" that would meet the limitations of the claims. "Stringent conditions" have not been also described in the specification and thus one of skill in the art would not be able to determine what polynucleotides would be considered to bind stringently, how long the polynucleotides might be, and whether applicant intended the claims to encompass complements to native chemokines, which would meet the limitations of the claim as written.

Applicants respond as follows:

The breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689 (C.C.P.A. 1971). Under § 2173.04 of the Manual of Patent Examining Procedure, if "the scope of the subject matter embraced is clear, and if the applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, second paragraph." Additionally, the definiteness of the claim language must be analyzed, not in a vacuum, but in light of:

(a) The content of the particular application disclosure;

(b) The teachings of the prior art; and

(c) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. M.P.E.P. § 2173.02.

Examiner states that the use of laboratory names to designate the proteins in claims 1-5, dependent claims 10-14, and claims 17 and 18 renders the claims vague and indefinite. The aforementioned proteins have been defined at page 2 of the specification, as belonging to the C-C, CXC or CX3C class of chemokines. Additionally, chemokines are well known in the art by their

common or laboratory names. The chemokine names disclosed in the specification represent the ordinary names of the respective chemokines, as used in the scientific literature. *See* http://www.ncbi.nlm.nih.gov/Omim/searchomim.html and the references cited at page 17, lines 21-25, and page 18, lines 1-2. The application disclosure identifies the proteins, and the scope of the claims must be interpreted in light of the disclosure.

Examiner also states that claims 1, 2, 6-14, 17, and 18 are indefinite in the recitation of "amino-terminal-modified". The term "amino-terminal-modified" is defined at page 17, lines 4-7, and Example 1 provides a working example of a specific type of amino-terminal modification. A person skilled in the art would readily identify the term "amino-terminal-modified" to refer to any kind of alteration, addition, insertion, deletion, mutation, substitution, replacement, or other modification, as defined at page 17, lines 4-7.

Lastly, Examiner states that the recitation of "amino-terminal fragment" and of "hybridizing under stringent conditions" renders claims 6-9 indefinite, since the length and specific characteristics of the "amino-terminal fragment" that would meet the limitations of the claim have not been described, and because the term "stringent conditions" has not been defined in the specification. Fragments of amino-terminal-modified chemokines are defined at page 20, lines 3-7 as follows: "Fragments of amino-terminal-modified chemokines are also encompassed by the present invention. Preferably, such fragments retain the desired activity of the amino-terminal-modified chemokine or modify to create a desired activity. Fragments of amino-terminal-modified chemokines may be in linear form or they may be cyclized using known methods." Stringent hybridization conditions are defined at page 22, lines 14-16 as follows: "Highly stringent

conditions include, for example, 0.2xSSC at 65°C; stringent conditions include, for example, 4xSSC at 65°C or 50% formamide and 4xSSC at 42°C."

RESPONSE TO REJECTION UNDER 35 U.S.C. § 102

Claims 1, 5 and 10-14 are rejected under 35 U.S.C. § 102 as being anticipated by prior art. In making the rejection, the Examiner states the following:

> Claims 1, 5 and 10-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Pelus et. al., U.S. patent no. 6080398, which claims priority to 1993 and Talmadge, U.S. patent no. 5627156, filed 1994. Pelus et. al. (see the whole document) teaches amino terminal truncations of Gro having enhanced bioactivity. Talmadge teaches N-terminally modified interleukin-8 peptides (column 4, lines 25-53). Since applicant includes "any kind of alteration, addition, insertion, deletion, mutation, substitution, replacement, or other modification" (page 17) in the definition of amino-terminal-modified-chemokine", these truncations are within the scope of the instant claims.
> Claim 5 is rejected under 35 U.S.C. 102(b) as being anticipated by Proudfoot et. al., J. Biol. Chem. Vol. 271, pp. 2599-2603, February 2, 1996. Proudfoot et. al. (see the whole document) teaches the production of a RANTES antagonist by retention of the initiating methionine and therefore anticipates the instant claim of polynucleotides encoding amino-terminal modified chemokines wherein the chemokines are selected from a group including RANTES.

Applicants respond as follows:

Examiner has rejected claims 1, 5 and dependant claims 10-14 under § 102(e) as being anticipated by Pelus *et. al.* and Talmadge. Without conceding to the propriety of Examiner's rejection, Applicants have amended claims 1 and 5 to include the claim limitations from claims 2, 3 and 4. The amendments render the § 102(e) rejection based on Pelus *et. al.* and Talmadge moot since Pelus *et. al.* and Talmadge teach only amino- and carboxy-terminal truncations of Gro and IL-8 respectively, and do not teach the N-terminal specific modifications claimed by Applicants in amended claims 1 and 5.

Examiner has also rejected claim 5 under § 102(b) as being anticipated by Proudfoot *et. al.*, because teaches the production of a RANTES antagonist by retention of the initiating

methionine, and therefore anticipates the instant claim of polynucleotides encoding amino-terminal modified chemokines wherein the chemokines are selected from a group including RANTES. Without conceding to the propriety of Examiner's rejections, Applicants have amended claim 5 to delete RANTES from the list of chemokines specified in claim 5.

CONCLUSION

Applicant has addressed all of the Examiner's rejections. In conjunction with the claim amendments and arguments above, Applicant believes that all of the claims are now in condition for allowance and respectfully requests that the Examiner grant such an action. If any questions or issues remain in the resolution of which the Examiner feels will be advanced by a conference with the Applicant's attorney, the Examiner is invited to contact the attorney at the number noted below.

It is believed that no fees are due as a result of this Reply. The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account No. 10-0447 (Reference No.: 50657-05302USP1).

PATENT APPLICATION
ATTORNEY DOCKET NO.: 50657-05301USP1

Respectfully submitted,

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